Chapter 1

SUMMARY STATEMENTS ON THE INTERRELATIONSHIPS OF CIGARETTE SMOKE, CARBOXYHEMOGLOBIN, SMOKERS AND NONSMOKERS

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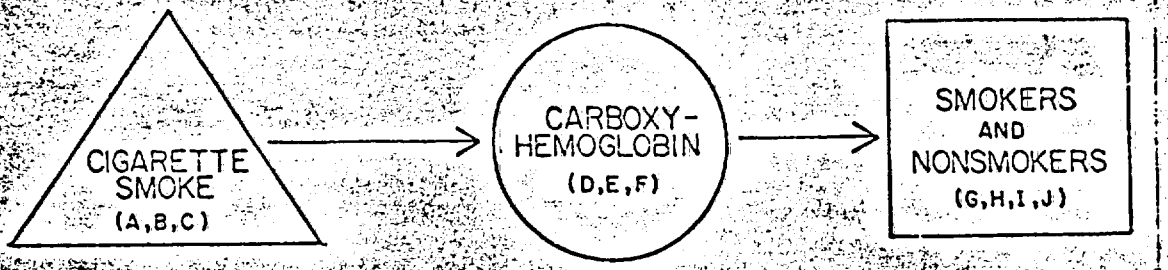
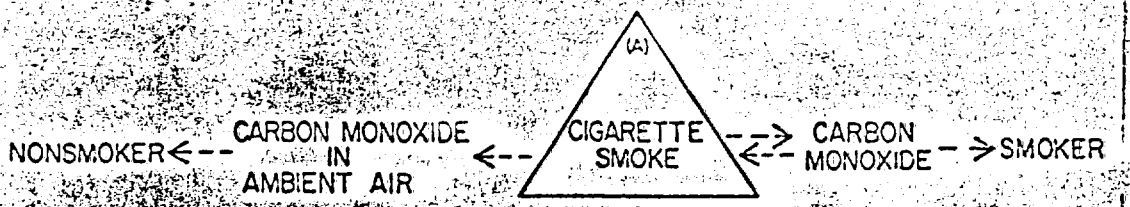


Since cigarette smoke contains carbon monoxide, it is suspected by some investigators that the carboxyhemoglobin level of smokers is elevated enough to adversely influence the cardiovascular system and central nervous system of smokers in general, to reduce the birth weight of infants and to cause respiratory symptoms in children of parents who smoke in particular. Even nonsmokers who are exposed to cigarette smoke are claimed to absorb carbon monoxide in sufficient amounts to be hazardous to their health.

The literature on the subject of cigarette smoke and carboxyhemoglobin is covered in this monograph to illustrate the invalid basis for the suspicion that smokers and nonsmokers suffer from the carbon monoxide contained in cigarette smoke. This general proposition is not supported by available facts which are summarized in ten statements, three relating to cigarette smoke (a, b, c), three to carboxyhemoglobin (d, e, f) and four to smokers and nonsmokers (g, h, i and j).

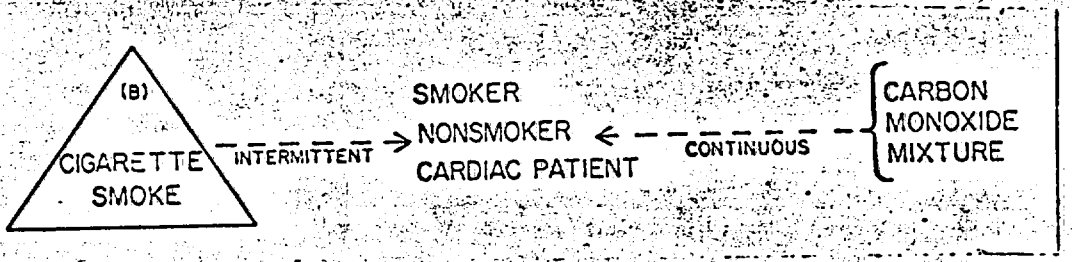


Summary Statement (a): A small and variable amount of carbon monoxide in cigarette smoke is absorbed by the smoker and even considerably less by the nonsmoker.

The total amount of carbon monoxide released from a burning cigarette varies from 5 to 80 ml, and the concentration in the cigarette smoke ranges from 0.5 to 8%. The 16-fold range in values is determined by the type of tobacco, speed of burning the cigarette and the amount of air diluting the smoke (see page 31). Of the amount of carbon monoxide inhaled with the cigarette smoke, about 54 to 87% is absorbed by the blood (see page 33).

It is difficult to estimate the amount of carbon monoxide that is inspired (mainstream smoke) separately from the amount that is not inhaled by the smoker (sidestream smoke). The quantity will depend on the amount and depth of inhalation and the frequency that the smoker inhales the mainstream smoke from the cigarette. Smokers vary in their smoking behavior, and an individual smoker has no set pattern of consuming cigarettes from hour to hour or from day to day. It is, therefore, misleading to attempt to quantitate the total amount of carbon monoxide that a smoker absorbs from cigarette smoke. The amount of carbon monoxide from cigarette smoke that is in the ambient air that a nonsmoker

is likely to inhale is even more variable because of the prevailing movement of air in an enclosure (see page 203). Estimations based on nicotine concentration in the ambient air and on the amount of nicotine absorbed by the nonsmoker indicate that the nonsmoker absorbs less than 1/100th of the cigarette smoke absorbed by the smoker (see page 209).



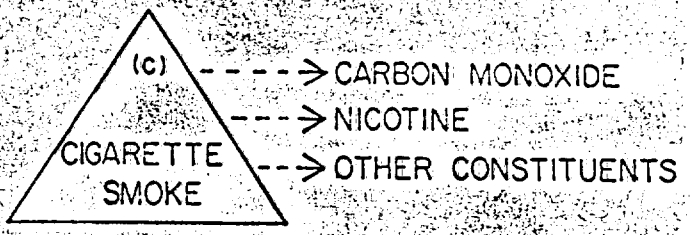
Summary Statement (b): Almost all the reported health effects of low levels of carbon monoxide were determined by continuous administration of a fixed concentration of carbon monoxide which is not applicable to the smoking situation, characterized by intermittent exposure to carbon monoxide.

The available information on the effects of low levels of carbon monoxide on smokers and nonsmokers, with or without heart disease, is largely based on experimental inhalation of the gas, continuously for many hours a day or without interruption daily for several weeks. These experiments were designed to determine occupational standard indoors (see page 155) and air quality standard for outdoors (see page 195).

The reported effects of inhalation of fixed concentrations of carbon monoxide on the cardiovascular system (see page 73) and the central nervous system (see page 104) do not necessarily apply to the intermittent exposure to carbon monoxide in the course of cigarette smoking. The theoretical analysis of the smoking

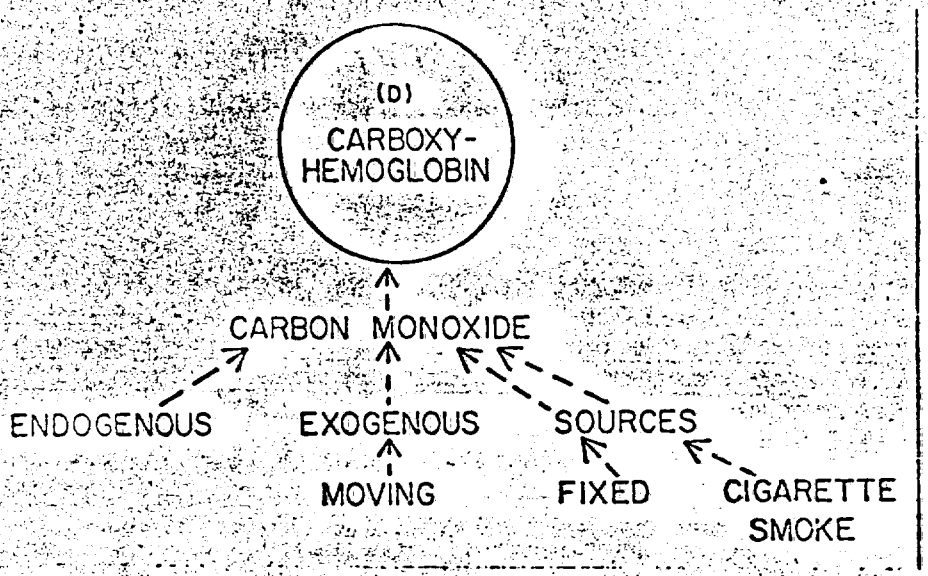
situation postulating a gradual accumulation of carbon monoxide in the body in the course of smoking several cigarettes in a day[1] is not supported by three groups of observations in smokers. First: The carboxyhemoglobin level of smokers at the end of the day is about the same as at the start (see page 35). Second: Smokers with their preexisting level of carboxyhemoglobin absorb less carbon monoxide[2-4] than nonsmokers indicating that uptake of the gas is not only determined by the inhaled concentration but by a complex group of factors that cannot be predicted by theoretical equations. Third: In animal experiments, the effects on the blood are more severe with continuous fixed concentrations of exposure than with intermittent exposure even though the carboxyhemoglobin level at the end is the same.

The smoking subject cannot be simulated by intermittent inhalation of carbon monoxide in air mixture. There is evidence that the smoker consumes cigarettes in a self-regulatory manner, to keep nicotine and carboxyhemoglobin levels in the blood constant. It appears that the smoker controls the amount of smoke inhaled, subconsciously to derive a level of carboxyhemoglobin that is optimal for the individual. This aspect of self-regulation of carbon monoxide as well as the adaptation to it needs further investigation.



Summary Statement (c): Because of the presence in cigarette smoke of nicotine, which has pharmacologic actions opposite to those of carbon monoxide, the effects of carbon monoxide alone cannot be equated to cigarette smoking.

It is taken for granted by some reviewers that the inhalation of low levels of carbon monoxide elicits the same effects as cigarette smoking. The fallacy in this belief is that cigarette smoke contains nicotine, which can antagonize the effects of carbon monoxide on the heart (see page 68) and the central nervous system (see page 110). One form of interaction has been excluded, i.e. the potential of carbon monoxide to depress drug-metabolizing enzymes in the liver in general, and, in particular, the metabolizing enzymes for nicotine. There are experiments which show that low levels of carbon monoxide do not depress metabolizing enzymes.[5,6] The other constituents of cigarette smoke are not covered in this review because there is no information on their interaction with carbon monoxide. The possibility of interaction exists until appropriate experiments for exclusion are completed.

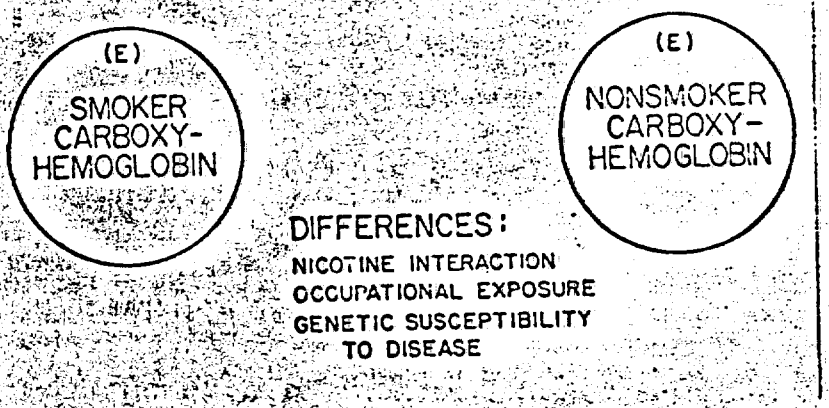


Summary Statement (d): The carboxyhemoglobin level in the blood of smokers represents not only carbon monoxide absorbed from cigarette smoke but also the carbon monoxide from exogenous sources and produced endogenously.

The uptake of carbon monoxide by the blood has been demonstrated during cigarette smoking (see page 33), inhalation of carbon monoxide mixtures in air (see page 104), exposure of workers to occupational sources of carbon monoxide (see page 148), exposure of workers and pedestrians to vehicular traffic (see page 165), and exposure to stationary or moving sources of carbon monoxide outdoors (see page 192) and indoors (see page 201). It is impossible to ascertain that a given amount of carboxyhemoglobin in the blood of smokers originates from cigarette smoke because the smoker is simultaneously exposed to other exogenous sources of carbon monoxide. Furthermore, there is an endogenous production of carbon monoxide which is represented by a variable fraction of the total carboxyhemoglobin in the blood of smokers and nonsmokers.[7,8] When nonsmokers and

smokers are compared in terms of carboxyhemoglobin level, it is not to establish the effect of smoking. The comparison cannot exclude smokers with a high level of endogenous formation of carbon monoxide and nonsmokers with low level of endogenous formation. Different exogenous exposures of smokers and nonsmokers can further complicate the deriving of any conclusion with respect to the effect of smoking alone.

Nit picking



Summary Statement (e): The difference in carboxyhemoglobin levels between smokers and nonsmokers is accompanied by differences not only in cigarette use but also in occupational exposure and genetic susceptibility to disease.

Although the mean values for carboxyhemoglobin levels in the blood of smokers are higher than those for nonsmokers, there is a considerable overlapping in individual values. The standard deviation for the mean of smokers is considerably wider than that of nonsmokers in comparisons of blood donors (see page 25), anginal patients (see page 51), pregnant women (see page 128), welders (see page 150), motor vehicle drivers (see page 169) and pedestrians (see page 193). The practice of characterizing smokers by a single mean value has led to considerable confusion because of the variability in exposure to sources of carbon monoxide of smokers.

The differences in the health of smokers and nonsmokers is explained usually by the smoking habit together with the difference in mean carboxyhemoglobin level. There are other factors that are difficult to exclude in accepting a causal relationship between smoking and elevated carboxyhemoglobin levels. First: Smokers

adjust their consumption of cigarettes to maintain a constant level of nicotine,[9] as well as a constant level of carboxyhemoglobin; any effects of carbon monoxide are antagonized by nicotine because of their opposite actions on the heart and central nervous system (see Summary Statement c). Second: Smokers are more likely to be exposed to occupational-related hazards than nonsmokers, because there is a higher incidence of smokers employed in those hazardous jobs than in other groups.[10] The higher incidence of diseases among smokers may be a reflection of the higher incidence in exposure. Third: The metabolism of carbon monoxide and associated environmental pollutants is influenced by hereditary[11] and constitutional factors,[12,13] which may be different between smokers and nonsmokers. This possibility is difficult to prove or disprove but it has to be considered as a likely explanation for the difference in health characteristics between smokers and nonsmokers.

More

(F)

CARBOXY-HEMOGLOBIN

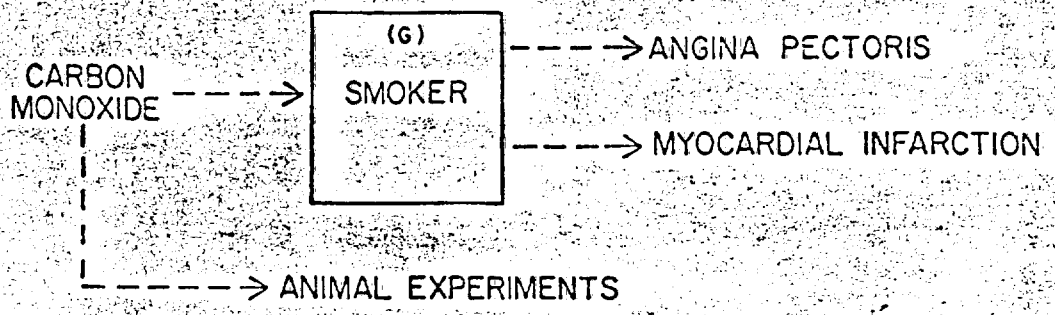
ADAPTATION OF:

ERYTHROCYTES
BONE MARROW
LIVER
HEART
CENTRAL NERVOUS SYSTEM

Summary Statement (f): In the interpretation of results of prolonged exposure to low levels of carbon monoxide, the development of adaptation to carboxyhemoglobin by smokers should be considered.

Adaptation or acclimatization to low concentration of carbon monoxide is a phenomenon that has been ignored in the consideration of the health effects of carbon monoxide in cigarette smoke. That continuous exposure to carbon monoxide will lead to increase in tolerance in man and animals has been explained by adaptation of the erythrocytes, bone marrow, liver, heart and central nervous system.[14-19] Investigations planned in the future should be designed to determine the degree of adaptation, not only to carbon monoxide but also to nicotine contained in cigarette smoke.

Some adaptation probably does occur

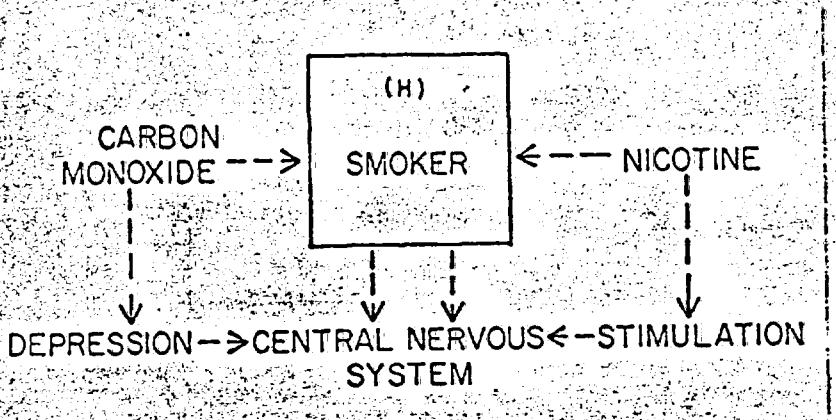


Summary Statement (g): The carboxyhemoglobin levels of cigarette smokers are not high enough to cause coronary heart disease.

The observations in patients with heart disease and in animals do not support the hypothesis that carboxyhemoglobin levels in cigarette smoke are high enough to provoke angina pectoris or cause myocardial infarction. The major shortcoming of the hypothesis is that the experimental procedure involves inhalation of carbon monoxide without nicotine. The nicotine in cigarette smoke produces cardiac actions opposite to those of carbon monoxide (see Chapter 3 beginning on page 46).

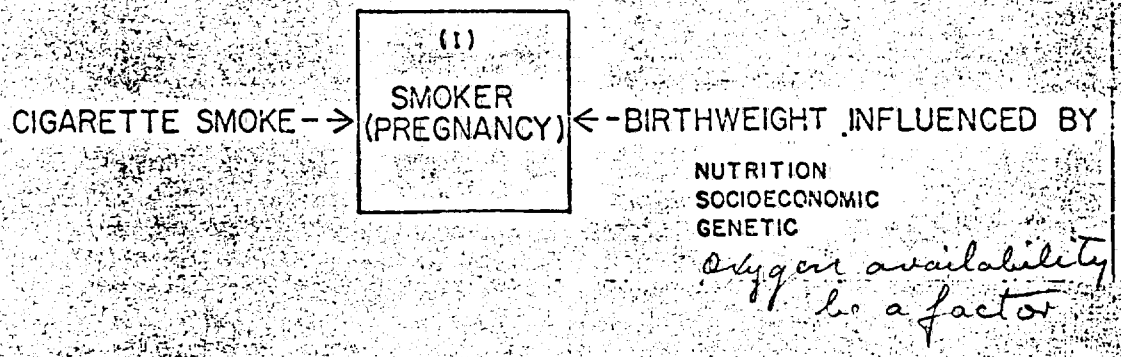
One topic not covered in Chapter 3 is the influence of carbon monoxide on the hemoglobin oxygen dissociation curve. The shift to the left with an elevation of carboxyhemoglobin means a decrease in oxygen release from the blood in the heart and tissues. It is important to point out that patients who develop heart disease have either a shift to the left or to the right and an abnormal hemoglobin is seen in patients with heart disease who are nonsmokers.[20-24] The appearance of an abnormal oxygen dissociation curve in smokers with heart disease cannot be caused by smoking alone since the same phenomenon is seen in patients who are nonsmokers.

Maybe



Summary Statement (h): It is unlikely that the carboxyhemoglobin levels of cigarette smokers are high enough to depress the central nervous system.

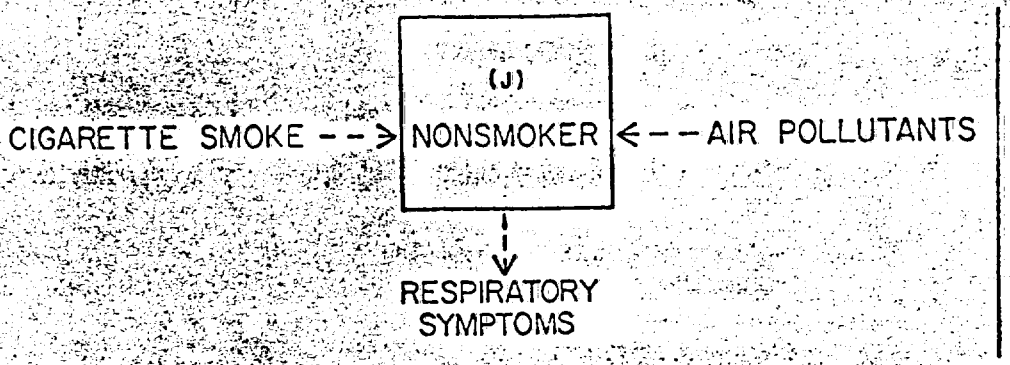
A review of the literature reveals that depression of the central nervous system by carbon monoxide is seen only when carboxyhemoglobin levels are above 20% saturation. The reports claiming a depression at levels below 20% are questionable and have not been confirmed. Since cigarette smokers rarely have a carboxyhemoglobin level reaching 20% saturation, a possible depressant influence of carbon monoxide on cerebral function can be excluded. Furthermore, nicotine absorbed by the smoker stimulates the central nervous system and can antagonize any depressant action of carbon monoxide (see Chapter 4 beginning on page 101).



Summary Statement (i): The contention that smoking during pregnancy causes an elevation in carboxyhemoglobin level high enough to reduce birth weight of the newborn is not supported by experimental and epidemiologic data.

In the interpretation of epidemiologic data relating to smoking in pregnancy, the following factors contribute to the low birth weight of infants of smoking mothers: nutrition, socioeconomic factors and inherited genetic characteristics of the mother. The strength of these factors in influencing the birth weight of the newborn are discussed in detail in this monograph (see Chapter 5 beginning on page 126). The contention that carboxyhemoglobin levels of smoking mothers is a cause of low birth weight is discredited by the results of epidemiologic studies and experiments in animals exposed to cigarette smoke. Such experiments do not duplicate the results of exposure of pregnant animals to carbon monoxide.

Not all that convincing.



Summary Statement (j): There is no evidence that the health of a nonsmoker is threatened when exposed to cigarette smoke in an enclosed environment.

Actual measurements of carbon monoxide and nicotine levels indoors do not show concentrations approaching occupational exposure standards. Nonsmokers exposed in chambers or nonventilated rooms filled with cigarette smoke do not develop cardiovascular reaction or respiratory symptoms. Subjective complaints of nonsmokers are a psychosocial reaction to the irritation of the mucosa by chemical components of cigarette smoke other than carbon monoxide (see Chapter 9 beginning on page 201).

Yes

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